

**AMENDMENTS TO THE SPECIFICATION**

**IN THE SPECIFICATION:**

**Page 1**

Please replace page 1 of the specification with the attached new Page 1 (amended sheet), located at the end of this Amendment.

Before line 1 of the specification, please insert the following new paragraph:

This Non-provisional application claims priority under 35 U.S.C. § 119(e) on U.S. Provisional Application No(s). 60/553,962 filed on March 18, 2004 and under 35 U.S.C. § 119(a) on Patent Application No(s). PA 2004 00454 filed in Denmark on March 22, 2004, the entire contents of which are hereby incorporated by reference.

## STEREOSELECTIVE SYNTHESIS OF VITAMIN D ANALOGUES

## FIELD OF THE INVENTION

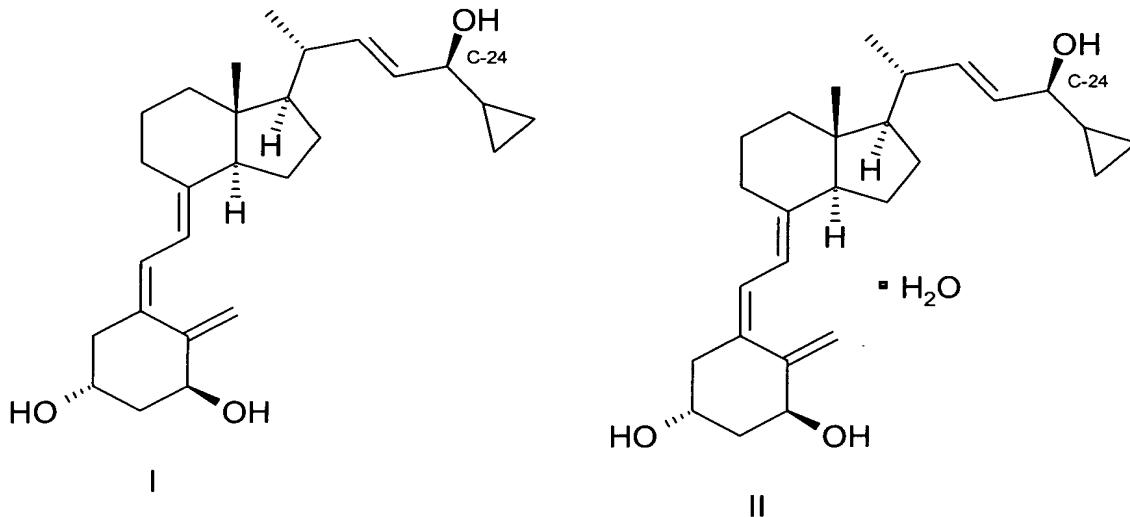
- 5 The present invention relates to methods of producing calcipotriol {(5Z, 7E, 22E, 24S)-24-cyclopropyl-9,10-secochola-5,7,10(19),22-tetraene-1 $\alpha$ -3 $\beta$ -24-triol} or calcipotriol monohydrate by stereoselective reduction. The present invention further provides novel intermediates and methods for the synthesis of the intermediates useful for producing calcipotriol or calcipotriol monohydrate.

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## BACKGROUND OF THE INVENTION

- Calcipotriol or calcipotriene (structure I) [CAS 112965-21-6] shows a strong activity in inhibiting undesirable proliferation of epidermal keratinocytes [F.A.C.M. Castelijns, M.J. 15 Gerritsen, I.M.J.J. van Vlijmen-Willems, P.J. van Erp, P.C.M. van de Kerkhof; Acta Derm. Venereol. 79, 11, 1999]. The efficiency of calcipotriol and calcipotriol monohydrate (II) in the treatment of psoriasis was shown in a number of clinical trials [D.M. Ashcroft *et al.*; Brit. Med. J. 320, 963-67, 2000] and calcipotriol is currently used in several commercial drug formulations.

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- In the preparation of calcipotriol, the specific stereochemistry for the hydroxyl group at C-24 is necessary for full expression of the biological activity. Under current 25 methodology, the required stereochemistry is introduced by one of the following methods:

**AMENDED SHEETS**